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ALL	14 same 13	961	L5
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ALL	dna or nucleic or gene	174407	L2
ALL	fusion or hybrid	184890	L1

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Document Number 1

Entry 1 of 961   File: USPT   Mar 14, 2000

US-PAT-NO: 6037329
DOCUMENT-IDENTIFIER: US 6037329 A
TITLE: Compositions containing nucleic acids and ligands for therapeutic treatment
DATE-ISSUED: March 14, 2000
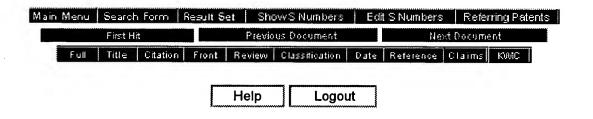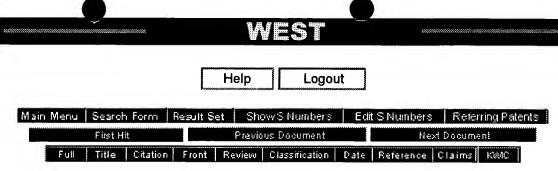US-CL-CURRENT: 514/44; 424/93.21, 435/320.1, 435/325, 435/455, 435/458, 435/69.1, 530/350, 536/23.1
APPL-NO: 8/ 718904
DATE FILED: September 24, 1996
PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS The application is a continuation-in-part of U.S. application Ser. No. 08/441,979, filed May 16, 1995, now abandoned; which is a continuation-in-part of U.S. application Ser. No. 08/213,446, filed Mar. 15, 1994, now abandoned; Ser. No. 08/213,447, filed Mar. 15, 1994, now abandoned; Ser. No. 08/297,961, filed Aug. 29, 1994, now abandoned; and Ser. No. 08/305,771, filed Sep. 13, 1994, now abandoned.

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Document Number 6

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Entry 6 of 961                    File: USPT                  Mar 14, 2000


DOCUMENT-IDENTIFIER: US 6036955 A
TITLE: Kits and methods for the specific coagulation of vasculature


BSPR:
Alternatively, such bispecific coagulating agents may be fusion proteins
prepared by molecular biological techniques, i.e., by joining a gene (or
cDNA) encoding a binding ligand or region to a gene (or cDNA) encoding a
coagulation factor. This is well known in the art and is further
described herein. Typically, an expression vector is prepared that
comprises, in the same reading frame, a DNA segment encoding the first
binding region operatively linked to a DNA segment encoding the
coagulation factor and expressing the vector in a recombinant host cell
so that it produces the encoded fusion protein.

DEPR:
In general, to prepare a fusion a protein one would join a DNA coding
region, such as a gene or cDNA, encoding a binding ligand or other
targeting region to a DNA coding region (i.e., gene or cDNA) encoding a
coagulation factor or coagulant binding region. This typically involves
preparing an expression vector that comprises, in the same reading
frame, a first DNA segment encoding the first binding region operatively
linked to a second DNA segment encoding the coagulation factor. The
sequences are attached in a manner such that translation of the total
nucleic acid yields the desired bispecific compounds of the invention.
Expression vectors contain one or more promoters upstream of the
inserted DNA regions that act to promote transcription of the DNA and to
thus promote expression of the encoded recombinant protein. This is the
meaning of "recombinant expression".
```
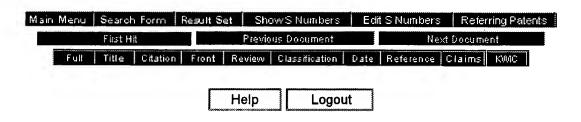
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Document Number 114

Entry 114 of 961   File: USPT   Nov 2, 1999

DOCUMENT-IDENTIFIER: US 5977307 A
TITLE: Transferrin receptor specific ligand-neuropharmaceutical agent
fusion proteins

DEPR:
The ligand-neuropharmaceutical agent fusion protein, which has both
ligand binding and neuropharmaceutical characteristics, can be produced
as a contiguous protein by using genetic engineering techniques. Gene
constructs can be prepared comprising DNA encoding the ligand fused to
DNA encoding the protein, polypeptide or peptide to be delivered across
the blood brain barrier. The ligand coding sequence and the agent coding
sequence are inserted in the expression vectors in a suitable manner for
proper expression of the desired fusion protein. The gene fusion is
expressed as a contiguous protein molecule containing both a ligand
portion and a neuropharmaceutical agent portion. For example, sequences
encoding neurotrophic agents such as NGF (nerve growth factor) or CNTF
(ciliary neurotrophic factor) can be fused with the sequence encoding
transferrin to create chimeric polypeptides that will be expressed and
subsequently transported across the BBB via the transferrin receptor.

DEPR:
The genetic engineering techniques are often used to insert linker DNA
sequences between the ligand and the neuropharmaceutical agent DNA
encoding sequences. These linker DNA sequences can be expressed as part
of the fusion protein. For example, specific segments of the constant
region of an antibody, including the hinge region, can be inserted
between the ligand and the neuropharmaceutical agent. These expressed
insertions serve to separate the ligand from the neuropharmaceutical
agent and may facilitate the proper folding of the expressed ligand or
agent into its proper conformation. When the insertions are segments
from the constant region of antibodies that are syngeneic to the host,
they have the added advantage of having reduced immunogenicity when
administered.

DEPR:
Such chimeric antibodies can readily be adapted to being part of the
fusion proteins of this invention. The DNA which contains the variable
region coding sequence can be fused to DNA which contains the
neuropharmaceutical agent coding sequence for subsequent expression as a
fusion protein. Likewise, the DNA which contains the variable region
coding sequence can be fused to DNA which contains the coding sequence
of a second ligand, if such an expressed fusion protein is desired. The
chimeric antibodies comprising constant and variable region portions
from two different species can easily be converted to fusion proteins of
this invention by inserting DNA encoding a neuropharmaceutical agent or
DNA encoding another ligand after a specific portion of constant region
encoding DNA. The subsequently expressed fusion protein will then
contain the variable region from one species, a desired portion of the
constant region from another species and a second ligand or the agent to
be transferred across the blood brain barrier.